L4 ANSWER 3 OF 3 USPATFULL
TI Methods of treating leukemia
AN 2002:199116 USPATFULL
TI Methods of treating leukemia
IN Gourdeau, Henriette, Montreal, CANADA
Giles, Francis J., Houston, TX, UNITED STATES
PA BioChem Pharma Inc., Laval, CANADA (non-U.S. corporation)
PI US 2002107225 A1 20020808
AI US 2002-46289 A1 20020116 (10)
RLI Division of Ser. No. US 2000-536459, filed on 28 Mar 2000, PENDING
PRAI US 1999-126734P 19990329 (60)
US 1999-126813P 19990330 (60)
DT Utility
FS APPLICATION
LREP MILLEN, WHITE, ZELANO & BRANIGAN, PC, 2200 CLARENDON BLVD, SUITE 1400, ARLINGTON, VA, 22201
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 629
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a novel method for treating leukemia and more particularly acute myelogenous leukemia (AML) in a host comprising administering to the host a therapeutically effective amount of a compound having the formula I: ##STR1##

wherein B is cytosine or 5-fluorocytosine and R is selected from the group comprising H, monophosphate, diphosphate, triphosphate, carbonyl substituted with a C.sub.1-6 alkyl, C.sub.2-6 alkenyl, C.sub.2-6 alkynyl, C.sub.6-10 aryl, and ##STR2##

wherein each Rc is independenty selected from the group comprising H, C.sub.1-6 alkyl, C.sub.2-6 alkynyl and an hydroxy protecting group; and

wherein said compound is substantially in the form of the (-) enantiomer.

SUMM . . . Approximately 40 different drugs are now being used in the treatment of leukemia. Some common combinations include cytarabine with either **doxorubicin** or daunorubicin or mitoxantrone or thioguanine, mercaptopurine with methotrexate, mitroxantrone with etoposide, asparaginase with vincristine, daunorubicin and prednisone, cyclophosphamide with. . .

SUMM [0010] (-)-.beta.-L-Dioxolane-Cytidine(.beta.-**L-OddC**) is also a nucleoside analogue that was first described as an antiviral agent by Belleau et al. (EP 337713) and. . .

SUMM [0027] In one embodiment, a compound of formula I is (-)-.beta.-L-Dioxolane-Cytidine (.beta.-**L-oddC**).

SUMM . . . the chemotherapeutic agents are selected from the group consisting of Asparaginase, Bleomycin, Busulfan, Carmustine, Chlorambucil, Cladribine, Cyclophosphamide, Cytarabine, Dacarbazine, Daunorubicin, **Doxorubicin**, Etoposide, Fludarabine, Gemcitabine, Hydroxyurea, Idarubicin, Ifosfamide, Lomustine, Mechlorethamine, Melphalan, Mercaptopurine, Methotrexate, Mitomycin, Mitoxantrone, Pentostatin, Procarbazine, 6-Thioguanine, Topotecan, Vinblastine, Vincristine, Dexamethasone,. . .

SUMM . . . In another embodiment, the chemotherapeutic agents are selected from the group consisting of Cytarabine, Etoposide, Mitoxantron, Cyclophosphamide, Retinoic acid, Daunorubicin, **Doxorubicin** and Idarubicin.

SUMM [0072] Still in another embodiment, the chemotherapeutic agent is **Doxorubicin**.

DETD Preparation of .beta.-**L-oddC**

DETD [0092] Compound #4: .beta.-**L-OddC**

DETD . . . distillation. The crude product was purified by flash chromatography on silica-gel (5% MeOH in EtOAc) to yield a white solid (b-**L-OddC**)(2.33 g; 86% overall yield, .alpha..sub.D.sup.22=-46.7.degree. (c=0.285; MeOH) m.p.=192-194.degree. C.). .sup.1H NMR (300 MHz,DMSO-d.sub.6) .delta. 3.63 (2H,dd,H-5'); 4.06 (2H,m,H-2'); 4.92 (1H,t,H-4');. . .

DETD Evaluation of .beta.-**L-oddC** in Patients with Advanced Leukemia.

DETD .beta.-**L-OddC/doxorubicin** Combination Study in a Human Leukemia (HL60) Xenograft Model

DETD [0095] A study was conducted to evaluate the synergistic or additive therapeutic effect of .beta.-**L-OddC** in combination with the currently known anticancer agent **Doxorubicin**. The model that was utilized is a survival model consisting of female SCID mice which are inoculated in the abdomen. . .

DETD [0096] 10 animals were used per group for .beta.-**L-oddC** alone, **Doxorubicin** alone and the combination of .beta.-**L-oddC** with **Doxorubicin**. Each groups received the drugs alone or in combination intravenously once daily for 5 consecutive days.

DETD [0098] In Table 1 below, we observe that the best treatment corresponds to the combination of .beta.-**L-oddC** with **Doxorubicin** at a dose of 2 mg/Kg. This combination extends the survival time of the mice substantially compared to either single agents .beta.-**L-OddC** and **Doxorubicin**.

TABLE 1

COMBINATION STUDY .beta.-**L-OddC/DOXORUBICIN** IN HUMAN LEUKEMIA (HL60)

Group of	Combination	Augmentation Survival Time
1	Saline i.p.	
2	.beta.-**L-OddC** 1 mg/kg	55%
3	**Doxorubicin** 0.2 mg/kg	25%
4	.beta.-**L-OddC** 1 mg/kg + **Doxorubicin** 0.2 mg/kg	55%
5	**Doxorubicin** 2 mg/kg	50%
6	.beta.-**L-OddC** 1 mg/kg. + **Doxorubicin** 2 mg/kg	100%

CLM What is claimed is:

20. The method according to claim 11, wherein the compound of formula I and the **doxorubicin** are administered sequentially.

21. The method according to claim 11, wherein the compound of formula I and the **doxorubicin** are administered simultaneously.

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CLMN Number of Claims: 29
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 769
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a novel method for treating a patient with cancer comprising administering to the patient a therapeutically effective amount of cisplatin and a compound having the formula I: ##STR1##

wherein B is cytosine or 5-fluorocytosine and R is selected from the group comprising H, monophosphate, diphosphate, triphosphate, carbonyl substituted with a C.sub.1-6 alkyl, C.sub.2-6 alkenyl, C.sub.2-6 alkynyl, C.sub.6-10 aryl, and ##STR2##

wherein each Rc is independently selected from the group comprising H, C.sub.1-6 alkyl, C.sub.2-6 alkenyl, C.sub.2-6 alkynyl and a hydroxy protecting group.

SUMM . . . (2001), 19(3), pp 762-771 and also Gourdeau et al Cancer Chemother. Pharmacol. (2001), 47(3), pp 236-240) that roxacitabine (.beta.-L-dioxolane cytidine, .beta.-**L-OddC**, Troxatyl.TM.), a nucleoside analogue, has shown to have potent activity in the treatment of various forms of cancers (e.g. solid. . .

SUMM [0029] In one embodiment, a compound of formula I is (-)-.beta.-L-Dioxolane-Cytidine (.beta.-**L-OddC**).

SUMM . . . comprising a therapeutically effective amount of cisplatin and a compound having formula I wherein the compound of formula I is .beta.-**L-OddC**.

SUMM . . . the further therapeutic agent is a chemotherapeutic agent chosen from Asparaginase, Bleomycin, Busulfan, Carmustine, Chlorambucil, Cladribine, Cyclophosphamide, Cytarabine, Dacarbazine, Daunorubicin, **Doxorubicin**, Etoposide, Fludarabine, Gemcitabine, Hydroxyurea, Idarubicin, Ifosfamide, Lomustine, Mechlorethamine, Melphalan, Mercaptopurine, Methotrexate, Mitomycin, Mitoxantrone, Pentostatin, Procarbazine, 6-Thioguanine, Topotecan, Vinblastine, Vincristine, Dexamethasone,. . .

SUMM . . . In another embodiment, the further therapeutic agent is a chemotherapeutic agent chosen from Cytarabine, Etoposide, Mitoxantron, Cyclophosphamide, Retinoic acid, Daunorubicin, **Doxorubicin** and Idarubicin.

SUMM [0043] In another embodiment, the further therapeutic agent is **Doxorubicin**.

SUMM . . . patient a therapeutically effective amount of cisplatin and a compound having formula I wherein the compound of formula I is .beta.-**L-OddC**.

SUMM . . . the further therapeutic agent is a chemotherapeutic agent chosen from Asparaginase, Bleomycin, Busulfan, Carmustine, Chlorambucil, Cladribine, Cyclophosphamide, Cytarabine, Dacarbazine, Daunorubicin, **Doxorubicin**, Etoposide, Fludarabine, Gemcitabine, Hydroxyurea, Idarubicin, Ifosfamide, Lomustine, Mechlorethamine, Melphalan,

Mercaptopurine, Methotrexate, Mitomycin, Mitoxantrone, Pentostatin, Procarbazine, 6-Thioguanine, Topotecan, Vinblastine, Vincristine, Dexamethasone,. . .

SUMM . . . treating cancer wherein the further therapeutic agent is a chemotherapeutic agent chosen from Cytarabine, Etoposide, Mitoxantron, Cyclophosphamide, Retinoic acid, Daunorubicin, **Doxorubicin** and Idarubicin.

SUMM [0065] In another embodiment, there is provided a method for treating cancer wherein the further therapeutic agent is **Doxorubicin**.

SUMM [0081] In another aspect, cisplatin and .beta.-**L-OddC** are administered in one twenty four hour period at intervals of every two to five weeks. In another embodiment, cisplatin and .beta.-**L-OddC** are adminstered consecutively at intervals of every two to five weeks.

SUMM [0102] In another embodiment, cisplatin and .beta.-**L-OddC** are administered in one twenty four hour period at intervals of every two to five weeks. In another embodiment, cisplatin and .beta.-**L-OddC** are administered consecutively at intervals of every two to five weeks.

SUMM [0103] In another embodiment, cisplatin and .beta.-**L-OddC** are administered in one twenty four hour period at intervals of every three to four weeks. In another embodiment, cisplatin and .beta.-**L-OddC** are administered consecutively at intervals of every three to four weeks.

DETD Preparation of .beta.-**L-OddC**

DETD [0115] Compound #4 .beta.-**L-OddC**

DETD . . . distillation. The crude product was purified by flash chromatography on silica-gel (5% MeOH in EtOAc) to yield a white solid (.beta.-**L-OddC**)(2.33 g; 86% overall yield, .alpha..sub.D.sup.22=-46.7.degree. (c=0.285; MeOH) m.p.=192-194.degree. C.). .sup.1H NMR (300 MHz, DMSO-d.sub.6) .delta. 3.63 (2H, dd, H-5'); 4.06. . .

DETD Evaluation of .beta.-**L-OddC** and Cisplatin in Cancer Patients

DETD [0117] A study was designed to determine the maximum tolerated dose of .beta.-**L-OddC** and cisplatin. The patients selected were adult patients with solid tumours that were refractory to standard therapies. They had an. . .

DETD . . . that one patient with metastatic non-small lung cancer (NSCLC) had a 42% reduction in disease extent after 2 courses of .beta.-**L-OddC**/cisplatin. Best responses so far include six patients with stable disease, 21 with progressive disease and six still unknown. The recommended dose for heavily pre-treated patients is .beta.-**L-OddC** 4.8 mg/m.sup.2 and cisplatin 50 mg/m.sup.2 administered every four weeks. The recommended dose for lightly pre-treated patients has not yet. . .

CLM What is claimed is:

5. The pharmaceutical combination according to claim 1 wherein a compound of formula I is (-)-.beta.-L-Dioxolane-Cytidine (.beta.-**L-OddC**).

11. The pharmaceutical combination according to claim 1 comprising a therapeutically effective amount of cisplatin and a compound of formula I wherein the compound of formula I is .beta.-**L-OddC** .

. . . claim 14 wherein the further therapeutic agent is a chemotherapeutic agent chosen from Cytarabine, Etoposide, Mitoxantron, Cyclophosphamide, Retinoic acid, Daunorubicin, **Doxorubicin** and Idarubicin.

17. A pharmaceutical combination according to claim 14 wherein the further therapeutic agent is **Doxorubicin**.

21. The pharmaceutical combination according to claim 14 wherein the

compound of formula I is .beta.-**L-OddC**.

25. The method according to claim 22 wherein said patient is administered a therapeutically effective amount of .beta.-**L-OddC** and Cisplatin.

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CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 629
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L4 ANSWER 1 OF 3 IFIPAT COPYRIGHT 2003 IFI
TI METHODS OF TREATING CANCER USING A COMBINATION OF DRUGS
AN 10283395 IFIPAT;IFIUDB;IFICDB
TI METHODS OF TREATING CANCER USING A COMBINATION OF DRUGS
INF Jolivet; Jacques, Laval, CA
IN Jolivet Jacques (CA)
PAF Shire BioChem Inc., Laval, CA
PA Shire BioChem Inc CA
AG MILLEN, WHITE, ZELANO & BRANIGAN, PC, 2200 CLARENDON BLVD, SUITE 1400, ARLINGTON, VA 22201, US
PI US 2003027799 A1 20030206
AI US 2002-107795 20020328
PRAI US 2001-279770P 20010330 (Provisional)
FI US 2003027799 20030206
DT Utility; Patent Application - First Publication
FS CHEMICAL
APPLICATION
CLMN 29
AB The present invention provides a novel method for treating a patient with cancer comprising administering to the patient a therapeutically effective amount of cisplatin and a compound having the formula I:

D R A W I N G

wherein B is cytosine or 5-fluorocytosine and R is selected from the group comprising H, monophosphate, diphosphate, triphosphate, carbonyl substituted with a C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C6-10 aryl, and

D R A W I N G

wherein each Rc is independently selected from the group comprising H, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl and a hydroxy protecting group.
ACLM . . . 5. The pharmaceutical combination according to claim 1 wherein a compound of formula I is (-)- beta -L-Dioxolane-Cytidine (beta -**L-OddC**).
. . . a therapeutically effective amount of cisplatin and a compound of formula I wherein the compound of formula I is beta -**L-OddC**.
. . . claim 14 wherein the further therapeutic agent is a chemotherapeutic agent chosen from Cytarabine, Etoposide, Mitoxantron, Cyclophosphamide, Retinoic acid, Daunorubicin, **Doxorubicin** and Idarubicin.
17. A pharmaceutical combination according to claim 14 wherein the further therapeutic agent is **Doxorubicin**.
21. The pharmaceutical combination according to claim 14 wherein the compound of formula I is beta -**L-OddC**.
25. The method according to claim 22 wherein said patient is administered a therapeutically effective amount of beta -**L-OddC** and Cisplatin.

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SUMM . . . comprising a therapeutically effective amount of cisplatin and a compound having formula I wherein the compound of formula I is .beta.-**L-OddC**.

SUMM . . . the further therapeutic agent is a chemotherapeutic agent chosen from Asparaginase, Bleomycin, Busulfan, Carmustine, Chlorambucil, Cladribine, Cyclophosphamide, Cytarabine, Dacarbazine, Daunorubicin, **Doxorubicin**, Etoposide, Fludarabine, Gemcitabine, Hydroxyurea, Idarubicin, Ifosfamide, Lomustine, Mechlorethamine, Melphalan, Mercaptopurine, Methotrexate, Mitomycin, Mitoxantrone, Pentostatin, Procarbazine, 6-Thioguanine, Topotecan, Vinblastine, Vincristine, Dexamethasone,. . .

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SUMM [0102] In another embodiment, cisplatin and .beta.-**L-OddC** are administered in one twenty four hour period at intervals of every two to five weeks. In another embodiment, cisplatin and .beta.-**L-OddC** are administered consecutively at intervals of every two to five weeks.

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DETD . . . that one patient with metastatic non-small lung cancer (NSCLC) had a 42% reduction in disease extent after 2 courses of .beta.-**L-OddC**/cisplatin. Best responses so far include six patients with stable disease, 21 with progressive disease and six still unknown. The recommended dose for heavily pre-treated patients is .beta.-**L-OddC** 4.8 mg/m.sup.2 and cisplatin 50 mg/m.sup.2 administered every four weeks. The recommended dose for lightly pre-treated patients has not yet. . .

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. . . claim 14 wherein the further therapeutic agent is a chemotherapeutic agent chosen from Cytarabine, Etoposide, Mitoxantron, Cyclophosphamide, Retinoic acid, Daunorubicin, **Doxorubicin** and Idarubicin.

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wherein B is cytosine or 5-fluorocytosine and R is selected from the group comprising H, monophosphate, diphosphate, triphosphate, carbonyl substituted with a C.sub.1-6 alkyl, C.sub.2-6 alkenyl, C.sub.2-6

6 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS
TI Effect of nucleoside analog BCH-4556 on prostate cancer growth and metastases in vitro and in vivo
AN 1998:518119 CAPLUS
DN 129:239582
TI Effect of nucleoside analog BCH-4556 on prostate cancer growth and metastases in vitro and in vivo
AU Rabbani, Shafaat A.; Harakidas, Penelope; Bowlin, Terry; Attardo, Giorgio
CS Department of Medicine, Physiology, and Oncology, McGill University and Royal Victoria Hospital, Montreal, QC, H3A 1A1, Can.
SO Cancer Research (1998), 58(15), 3461-3465
CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
AB Prostate carcinoma is a common malignancy among males that results in high morbidity and mortality. Here, we have evaluated the capacity of nucleoside analog BCH-4556 [.beta.-L-(-)-dioxolane-cytidine] to control prostate cancer progression in our syngeneic model of rat prostate cancer using the rat prostate cancer cell line Dunning R3227 Mat Ly Lu. Different concns. (50 .mu.M-1 mM) of BCH-4556 resulted in a marked decrease and, eventually, a complete arrest of Mat Ly Lu cell growth in vitro. Cells were inoculated via intracardiac (i.c.) route into the left ventricle or by s.c. injection into the right flank of male Copenhagen rats. Following i.c. inoculation, exptl. animals were treated with 75 mg/kg BCH-4556 twice a day or with vehicle alone for 6 consecutive days, starting from day 1 or day 3 post-tumor cell inoculation. Control and exptl. animals were monitored for the development of tumor metastases. Treatment with BCH-4556 did not significantly change the development of skeletal metastases and, hence, the time of development of hind limb paralysis. Exptl. animals, however, did show a marked redn. in the incidence and size of tumor metastases at the adrenal glands. Following the development of palpable tumors after s.c. injection of Mat Ly Lu cells on day 8 post tumor cell inoculation, animals were treated i.p. with 25-75 mg/kg BCH-4556 twice a day or with vehicle alone for 6 consecutive days. Control animals developed large primary tumors and macroscopic metastasis to lungs, lymph nodes, kidneys, and spleen. In contrast, exptl. animals receiving BCH-4556 showed a marked decrease in tumor vol. and metastases after the last injection of BCH-4556. The max. dose of BCH-4556 (75 mg/kg twice a day) caused a complete arrest in tumor growth that was maintained for up to 4-6 days without any evidence of cytotoxicity. These antitumor effects of BCH-4556 were more marked than those of doxorubicin in blocking tumor growth in this model of prostate cancer, and it continued to be effective following three cycles of treatment, without manifesting any signs of drug resistance.
RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT **23214-92-8**, Doxorubicin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparative study; effect of nucleoside analog BCH-4556 on prostate cancer growth and metastases in vitro and in vivo)
IT **145918-75-8**, BCH-4556
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of nucleoside analog BCH-4556 on prostate cancer growth and metastases in vitro and in vivo)

=>

L6 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS
TI Methods of treating leukemia with cytosine dioxolane or fluorocytosine dioxolane derivative
AN 2000:706966 CAPLUS
DN 133:276325
TI Methods of treating leukemia with cytosine dioxolane or fluorocytosine dioxolane derivative
IN Gourdeau, Henriette; Giles, Francis J.
PA Biochem Pharma Inc., Can.
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000057861	A2	20001005	WO 2000-CA334	20000328
	WO 2000057861	A3	20010308		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1165096	A2	20020102	EP 2000-913985	20000328
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	BR 2000009378	A	20020108	BR 2000-9378	20000328
	JP 2002540142	T2	20021126	JP 2000-607612	20000328
	NO 2001004727	A	20011108	NO 2001-4727	20010928
	US 2002107225	A1	20020808	US 2002-46289	20020116
PRAI	US 1999-126734P	P	19990329		
	US 1999-126813P	P	19990330		
	US 2000-536459	A3	20000328		
	WO 2000-CA334	W	20000328		

OS MARPAT 133:276325
AB A method for treating leukemia, esp. acute myelogenous leukemia, comprises administering a therapeutically effective amt. of I (B = cytosine, 5-fluorocytosine; R = H, monophosphate, diphosphate, triphosphate, carbonyl substituted with a C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C6-10 aryl, and P(:O)(ORc)2; Rc = H, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, OH protecting group), wherein the compd. is substantially in the form of the (-) enantiomer.
IT **145918-75-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cytosine dioxolane or fluorocytosine dioxolane deriv. for leukemia treatment)
IT 9014-42-0, Thrombopoietin 11096-26-7, Erythropoietin **23214-92-8**, Doxorubicin 62683-29-8, Colony-stimulating factor 83869-56-1, GM-CSF 113427-24-0 121181-53-1, Filgrastim 121584-18-7, PSC 833 123774-72-1, Sargramostim 143011-72-7, G-CSF 174722-31-7, Rituxan 220578-59-6, Mylotarg
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytosine dioxolane or fluorocytosine dioxolane deriv. for leukemia treatment)

L6 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS
TI Effect of nucleoside analog BCH-4556 on prostate cancer growth and metastases in vitro and in vivo
AN 1998:518119 CAPLUS
DN 129:239582
TI Effect of nucleoside analog BCH-4556 on prostate cancer growth and metastases in vitro and in vivo
AU Rabbani, Shafaat A.; Harakidas, Penelope; Bowlin, Terry; Attardo, Giorgio
CS Department of Medicine, Physiology, and Oncology, McGill University and Royal Victoria Hospital, Montreal, QC, H3A 1A1, Can.
SO Cancer Research (1998), 58(15), 3461-3465
CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
AB Prostate carcinoma is a common malignancy among males that results in high morbidity and mortality. Here, we have evaluated the capacity of nucleoside analog BCH-4556 [.beta.-L-(-)-dioxolane-cytidine] to control prostate cancer progression in our syngeneic model of rat prostate cancer using the rat prostate cancer cell line Dunning R3227 Mat Ly Lu. Different concns. (50 .mu.M-1 mM) of BCH-4556 resulted in a marked decrease and, eventually, a complete arrest of Mat Ly Lu cell growth in vitro. Cells were inoculated via intracardiac (i.c.) route into the left ventricle or by s.c. injection into the right flank of male Copenhagen rats. Following i.c. inoculation, exptl. animals were treated with 75 mg/kg BCH-4556 twice a day or with vehicle alone for 6 consecutive days, starting from day 1 or day 3 post-tumor cell inoculation. Control and exptl. animals were monitored for the development of tumor metastases. Treatment with BCH-4556 did not significantly change the development of skeletal metastases and, hence, the time of development of hind limb

L6 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2003 ACS
TI Methods of treating cancer using a combination of cisplatin and a dioxolane nucleoside
AN 2002:777700 CAPLUS
DN 137:288983
TI Methods of treating cancer using a combination of cisplatin and a dioxolane nucleoside
IN Jolivet, Jacques
PA Shire Biochem Inc., Can.
SO PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002078678	A2	20021010	WO 2002-CA439	20020328
	WO 2002078678	A3	20030327		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	US 2003027799	A1	20030206	US 2002-107795	20020328
PRAI	US 2001-279770P	P	20010330		

OS MARPAT 137:288983
AB The invention provides a method for treating a patient with cancer, comprising administering to the patient a therapeutically effective amt. of cisplatin and I (B = cytosine, 5-fluorocytosine; R = H, monophosphate, diphosphate, triphosphate, carbonyl substituted with C1-6 alkyl, etc.). Prepn. of (-)-.beta.-L-dioxolane-cytidine is described.
IT **145918-75-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cisplatin-dioxolane nucleoside combination for treating cancer)
IT 50-18-0, Cyclophosphamide 147-94-4, Cytarabine 302-79-4, Retinoic acid 15663-27-1, Cisplatin 20830-81-3, Daunorubicin **23214-92-8**, Doxorubicin 33419-42-0, Etoposide 58957-92-9, Idarubicin 65271-80-9, Mitoxantrone 121584-18-7, PSC 833 467418-82-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cisplatin-dioxolane nucleoside combination for treating cancer)

L6 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS
TI Methods for enhancing antibody-induced cell lysis and treating cancer
AN 2001:935435 CAPLUS
DN 136:84677
TI Methods for enhancing antibody-induced cell lysis and treating cancer
IN Weiner, George; Hartmann, Gunther
PA University of Iowa Research Foundation, USA
SO PCT Int. Appl., 312 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 2001097843 A2 20011227 WO 2001-US20154 20010622
WO 2001097843 A3 20030123
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
US 2003026801 A1 20030206 US 2001-888326 20010622
EP 1296714 A2 20030402 EP 2001-948684 20010622
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRAI US 2000-213346P P 20000622
WO 2001-US20154 W 20010622
AB The invention relates to methods and products for treating cancer. In particular the invention relates to combinations of nucleic acids and antibodies for the treatment and prevention of cancer. The invention also relates to diagnostic methods for screening cancer cells.
IT 50-07-7, Mitomycin C 50-18-0, Cyclophosphamide 50-76-0, Dactinomycin 50-91-9, Floxuridine 51-21-8, 5-Fluorouracil 52-24-4, Thiotepa 53-19-0, Mitotane 55-86-7, Mechlorethamine hydrochloride 55-98-1,

L3 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2003 ACS
TI Beta-L-(-)-dioxolane cytidine (.beta.-L-(-)-odd) as a potent compound for the treatment of cancer
AN 1997:757879 CAPLUS
DN 128:97389
TI Beta-L-(-)-dioxolane cytidine (.beta.-L-(-)-odd) as a potent compound for the treatment of cancer
AU Grove, K. L.; Guo, X.; Liu, S-H.; Kukhanova, M.; Chu, C-K.; Cheng, Y-C.
CS Yale School of Medicine, Dept. of Pharmacology, New Haven, CT, 06520, USA
SO Nucleosides & Nucleotides (1997), 16(7-9), 1229-1233
CODEN: NUNUD5; ISSN: 0732-8311
PB Marcel Dekker, Inc.
DT Journal
LA English
AB **L**-(-)-**OddC** is the first nucleoside analog with the unnatural L-configuration and the first chain-terminator shown to have anti-cancer activity. This compd. was highly active against solid tumor growth in several human xenograft models **L**-(-)-**OddC** exerts its activity be terminating DNA chain elongation after its incorporation.
RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB **L**-(-)-**OddC** is the first nucleoside analog with the unnatural L-configuration and the first chain-terminator shown to have anti-cancer activity. This compd. was highly active against solid tumor growth in several human xenograft models **L**-(-)-**OddC** exerts its activity be terminating DNA chain elongation after its incorporation.

L3 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2003 ACS
TI Synthesis and anti-HIV activity of 2',3'-dideoxy-2'-fluoro-L-threo-pentofuranosyl nucleosides
AN 1997:486036 CAPLUS
TI Synthesis and anti-HIV activity of 2',3'-dideoxy-2'-fluoro-L-threo-pentofuranosyl nucleosides
AU Cavalcanti, Socrates C. H.; Cheng, Yung-Chi; Chu, Chung K.
CS College Pharmacy, University Georgia, Athens, GA, 30602-2352, USA
SO Book of Abstracts, 214th ACS National Meeting, Las Vegas, NV, September 7-11 (1997), CARB-080 Publisher: American Chemical Society, Washington, D. C.
CODEN: 64RNAO
DT Conference; Meeting Abstract
LA English
AB Little attention had been given to L-nucleosides until the finding of (-)-(2R,5S)-1-[(2-Hydroxymethyl)oxathiolan-5-yl]cytosine (3TC). Since then, several L-nucleosides such as FTC, L-FMAU and **L**-**OddC** have been discovered as promising antiviral and anticancer agents. These L-nucleosides are undergoing various stages of preclin. and clin. evaluations. In view of these facts, it was of interest to synthesize 2'-fluorinated L-nucleosides as shown below. In this presentation we report the synthesis and biol. activity of 2',3'-dideoxy-2'-fluoro-L-threo-pentofuranosyl nucleosides as potential anti-HBV agents.
AB Little attention had been given to L-nucleosides until the finding of (-)-(2R,5S)-1-[(2-Hydroxymethyl)oxathiolan-5-yl]cytosine (3TC). Since then, several L-nucleosides such as FTC, L-FMAU and **L**-**OddC** have been discovered as promising antiviral and anticancer agents. These L-nucleosides are undergoing various stages of preclin. and clin. evaluations. In view of these facts, it was of interest to synthesize 2'-fluorinated L-nucleosides as shown below. In this presentation we report the synthesis and biol. activity of 2',3'-dideoxy-2'-fluoro-L-threo-pentofuranosyl nucleosides as potential anti-HBV agents.

DN 124:215
TI L- and D-enantiomers of 2',3'-dideoxycytidine 5'-triphosphate analogs as substrates for human DNA polymerases. Implications for the mechanism of toxicity
AU Kukhanova, Marina; Liu, Shwu-Huey; Mozzherin, Dmitry; Lin, Tai-Shun; Chu, Chung K.; Cheng, Yung-Chi
CS Dep. Pharmacology, Yale Univ. Sch. Med., New Haven, CT, 06510, USA
SO Journal of Biological Chemistry (1995), 270(39), 23055-9
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Bio logy
DT Journal
LA English
AB 5'-Triphosphates of .beta.-D and .beta.-L-enantiomers of

English

AB .beta.-L-Dioxolane-cytidine (**L-OddC**, BCH-4556, Troxacitabine) is a novel unnatural stereochem. nucleoside analog that is under phase II clin. study for cancer treatment. This nucleoside analog

fluoromethylene)cytidine, MDL 101731, Tezacitabine); troxacitabine (.beta.-L-dioxolane cytidine, L-(-)-deoxy-3'-oxacytidine, BCH4556, **L-OddC**); CNDAC; 3'-Ethynylcytidine (ECyd, TAS-106); clofarabine,(Cl-F-ara-A, CAFdA); and nelarabine (2-amino-9-.beta.-D-arabinofuranosyl-6-methoxy-9H-purine, Compd. 506U).

g, troxacitabine (**L**-(-)-**OddC**,
BCH-4556), in patients with refractory leukemia. Study participants were patients with refractory or relapsed acute myeloid (AML) or

kinase 9001-59-6, Pyruvate kinase 9001-83-6, 3-Phosphoglycerate kinase
69256-17-3, D-FMAU 95058-81-4, DFdC 121154-51-6, L-DdC 134678-17-4,
L-SddC 145918-75-8, **L-OddC** 163252-36-6
181785-84-2, L-Fd4C
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(phosphorylation of pyrimidine deoxynucleoside analog diphosphates:

For example, a beneficial effect was obtained when the combination of (-)-.beta.-L-dioxolane-cytidine (.beta.-**L-OddC**) with Ara-C was used in refractory/relapsed leukemia patients, including the patients who were previously treated with Ara-C. The results equate to a 22% (11/49) response rate achieved using this combination.